The opinion in support of the decision being entered today is not binding precedent of the Board.

Paper 54

Filed by: Trial Section Merits Panel
Box Interference
Washington, D.C. 20231
Tel: 703-308-9797
Fax: 703-305-0942

Filed: February 12, 2003

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

GENCELL S.A.

Junior Party
U.S. Patent 6,127,175

v.

IMRE KOVESDI, DOUGLAS E. BROUGH, DUNCAN L. MCVEY, JOSEPH T. BRUDER and ALENA LIZONOVA

Junior Party,
Application 08/258,416

v.

GENCELL S.A.

Senior Party
Application 08/397,225

Patent Interference No. 104,829 (CAS)

Before: TORCZON, SPIEGEL and GARDNER LANE, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

MEMORANDUM OPINION and ORDER
(Decision on preliminary and miscellaneous motions)

I. Introduction

Interference 104,829 involves recombinant replication-defective[1] adenoviral vectors[2] wherein one or more essential functions[3] of at least[4] adenoviral early gene regions[5] E2 ("ΔE2") or E4 ("ΔE4") or both ("ΔE2,ΔE4") are nonfunctional and complementing cells[6] therefore.

The parties have filed two joint motions. Joint preliminary motion 1 seeks (i) to add Proposed Count 7 directed to a cell line which complements *in trans* a deficiency in

---

[1] A replication-defective [or deficient] viral vector is a viral vector that is unable to replicate due to deficiencies in gene functions essential for replication (i.e., generation of viral progeny) to occur. Such viral vectors are able to replicate in complementing cell lines that provide the missing gene functions *in trans* or with the aid of a helper virus.

[2] An adenoviral vector is an adenovirus that can carry a heterologou nucleic acid sequence (i.e., a transgene) into a suitable host cell. A transgene is a gene that is not normally present in a cell or viral vector, also called a heterologous or foreign gene.

[3] An essential gene is a gene that codes for a function necessary for cell or viral viability or normal growth. Adenovirus essential gene functions are encoded by, e.g., the adenoviral early regions (e.g., the E1, E2 and E4 regions), late regions (e.g., the L1-L5 regions), genes involved in viral packaging, and virus-associated RNAs (e.g., VA-RNA I and/or VA-RNA-II). The E3 region is not required for adenoviral growth in culture.

[4] For simplicity, the expressions ΔE2, ΔE4 and ΔE2,ΔE4 as used herein are intended to encompass recombinant replication-defective adenoviruses and adenoviral vectors wherein the E3 region and/or essential functions of the E1 region are also non-functional, e.g., because a part or all of the region has been deleted.

[5] The early region is an area of the adenoviral genome that contains adenovirus genes expressed before the onset of viral DNA replication. The early region is divided into the E1A, E1B, E2A, E2B, E3 and E4 regions.

[6] A complementing cell is a cell that enables growth of viral vectors deficient in gene functions essential for growth by providing the missing gene function(s) *in trans*. The 293 cell line, for example, is a permanent cell line of primary human embryonal kidney cells transformed by sheared human adenovirus type 5 (Ad 5) DNA that expresses the adenoviral E1A and E1B genes.

one or more essential gene functions in each of two or more early gene regions[7] of an adenoviral genome selected from the group consisting of E1, E2A and E4, *wherein the cell line comprises open reading frame[8] 6 (ORF6) and no other ORF of the E4 region,* (ii) to designate Kovesdi claims 39, 45, 48, 51 and 94 as not corresponding to present Counts 4 and 6, and (iii) to designate Kovesdi claims 39, 45, 48, 51 and 94 as well as Vigne claim 19 as corresponding to Proposed Count 7. Joint preliminary motion 2 seeks to designate Vigne claims 17 and 18 as corresponding to Count 4. Joint motion 2 also seeks to designate Vigne claim 19 as corresponding to Count 4 if it is not designated as corresponding to Proposed Count 7. We deny joint motion 1 and grant joint motion 2.

Party Gencell has filed two miscellaneous motions for extensions of time to reply, which have been previously granted (see Papers 22 and 27). Party Gencell has filed five preliminary motions. Gencell preliminary motion 1 seeks (i) to substitute Counts 1, 3, 4 and 6 with Proposed counts 1, 3, 4 and 6, (ii) to cancel Perricaudet '225 claims 21, 22, 24 and 33, (iii) to amend Perricaudet '225 claims 1, 2 and 11, (iv) to add new claims 43-64 to Perricaudet '225 and (v) to obtain judgment that there is no interference-in-fact between Perricaudet '225 claim 1 and Kovesdi's claims. Gencell preliminary motions 2 through 5 seek benefit of the filing dates of Gencell's priority PCT and French applications for the subject matter of Proposed Counts 1, 3, 4 and 6, respectively.

---

[7] The early region is an area of the adenoviral genome that contains adenoviral genes expressed before the onset of viral DNA replication. The early region is divided into the E1A, E1B, E2A, E2B, E3 and E4 regions.

[8] An open reading frame is a stretch of nucleic acid triplets, each triplet representing an amino acid, contained between an initiator codon and a terminator codon .

Gencell preliminary motion 1 is denied without prejudice to the APJ (Administrative Patent Judge) taking further appropriate action. Gencell preliminary motions 2 through 5 are dismissed without prejudice.

Party Kovesdi has filed a preliminary motion to amend Kovesdi claim 19, contingent upon the grant of joint preliminary motion 1. The preliminary motion is dismissed as moot. Party Kovesdi also filed a miscellaneous motion requesting Gencell to elect between its commonly owned patent (Vigne) and application (Perricaudet) for continuing in the interference. The miscellaneous motion was deferred until the count(s) in the interference were definite, i.e., until after a decision on preliminary motions (Paper 32).

II. Findings of fact

A. Junior party Vigne/Gencell

F1. Junior party, Emmanuelle Vigne, Michel Perricaudet, Jean-François Dedieu, Cécile Orsini, Patrice Yeh, Martine Latta and Edouard Prost (**Vigne/Gencell**), is involved in the interference on the basis of U.S. Patent 6,127,175 (Vigne '175), issued October 3, 2000, based on U.S. application 08/875,223 (Vigne '223), filed July 17, 1997.

F2. Vigne '175 has been accorded benefit for the purpose of priority of

(i) PCT application PCT/FR96/00088, filed January 19, 1996,

(ii) FR application 95/10541, filed September 8, 1995,

(iii) FR application 95/06532, filed June 1, 1995 and

(iv) FR application 95/00747, filed January 20, 1995.

F3. Vigne '175 is assigned to Gencell S.A.

B. Junior party Kovesdi

F4. Junior party, Imre Kovesdi, Douglas E. Brough, Duncan L. McVey, Joseph T. Bruder and Alena Lizonova (**Kovesdi**), is involved in the interference on the basis of U.S. application 08/258,416 (Kovesdi '426), filed June 10, 1994.

F5. Kovesdi '426 is assigned to Genvec.

C. Senior party Perricaudet/Gencell

F6. Senior party, Michel Perricaudet, Emmanuelle Vigne and Patrice Yeh (**Perricaudet/Gencell**), is involved in the interference on the basis of U.S. application 08/397,225 (Perricaudet '225), filed March 28, 1995.

F7. Perricaudet '225 has been accorded benefit for the purpose of priority of

(i) PCT application PCT/FR94/00851, filed July 8, 1994,

(ii) FR application 94/04590, filed April 18, 1994 and

(iii) FR application 93/08596, filed July 13, 1993.

F8. Perricaudet '225 is assigned to Gencell S.A.

D. Counts and claims of the parties

F8. The interference is defined by six (6) counts. Counts 1, 3 and 5 are directed to recombinant adenoviral vectors unable to replicate due to deficiencies in essential gene functions of the E2, E4 and both E2 and E4 regions, respectively. Counts 2, 4 and 6 are directed to the corresponding complementing cell lines therefor.

F9. Count 1 is defined by Kovesdi claim 57 or Kovesdi claim 72 or Perricaudet claim 35.

F10. Kovesdi claim 57 reads:

57. An adenoviral vector that requires, for replication, complementation *in trans* of one or more essential gene functions of each of at least the E1 and E2A regions of the adenoviral genome, which vector has been prepared using the cell line of claim 41.

F11. Kovesdi claim 72 reads:

72. The adenoviral vector of claim 68, wherein said vector is deficient in one or more essential gene functions in at least the E1 and E2A regions of the adenoviral genome.

F12. Perricaudet claim 35 reads:

35. A replication defective recombinant adenovirus comprising
ITR sequences,
an encapsulation sequence,
a heterologous DNA sequence, and
an E4 region,
wherein the E4 region is the sole adenoviral region.

F13. Count 2 is defined by Kovesdi claim 41 or Perricaudet claim 26.

F14. Kovesdi claims 36 and 41 read:

36. A cell line that complements *in trans* an adenoviral vector having an adenoviral genome, said genome being deficient in one or more essential gene functions of each of two or more adenoviral early regions selected from the group consisting of the E1, E2A, and E4 regions of said adenoviral genome, wherein nucleic acid sequences in said cell line encoding products complementing for said essential gene functions of said E2A and E4 regions of the adenoviral genome are operably linked to inducible promoters or repressible promoters, and wherein said cell line is derived from HEK 293 cells or A549 cells.

41. The cell line of claim 36, wherein said vector is deficient in one or more essential gene functions of at least the E1 and E2A regions of the adenoviral genome.

F15. Perricaudet claims 19 and 26 read:

19. A cell line comprising, integrated into its genome, adenovirus genes necessary to complement the replication defective recombinant

adenovirus according to claim 1, wherein one of the complementing genes is under the control of an inducible promoter.

26. The cell line according to claim 19, comprising a gene encoding the 72 K protein of E2, wherein the 72 K protein encoding gene is placed under the control of an inducible promoter.

F16. Count 3 is defined by Kovesdi claim 53 or Kovesdi claim 70 or Vigne claim 33 or Perricaudet claim 34.

F17. Kovesdi claim 53 reads:

53. An adenoviral vector that requires, for replication, complementation *in trans* of one or more essential gene functions of each of at least the E1 and E4 regions of the adenoviral genome, which vector has been prepared using the cell line of claim 37.

F18. Kovesdi claim 70 reads:

70. The adenoviral vector of claim 68, wherein said vector is deficient in one or more essential gene functions in at least the E1 and E4 regions of the adenoviral genome.

F19. Vigne claim 33 reads:

33. A defective recombinant adenovirus ΔE1,ΔE4, wherein all or part of the E1 region and the whole of the E4 region, chosen from the group consisting of Ad5 nucleotides 33466-35355 and 33093-35355, or the corresponding nucleotides from Ad2, Ad7 or Ad12, are deleted.

F20. Perricaudet claim 34 reads:

34. A replication defective recombinant adenovirus comprising
ITR sequences,
an encapsulation sequence,
a heterologous DNA sequence, and an E2 region,
wherein the E2 region is the sole adenoviral early region.

F21. Count 4 is defined by Kovesdi claim 38 or Vigne claim 1 or Perricaudet claim 22.

F22. Kovesdi claims 37 and 38 read (see F14 for Kovesdi claim 36):

37. The cell line of claim 36, wherein said vector is deficient in one or more essential gene functions of at least the E1 and E4 regions of the adenoviral genome.

38. The cell line of claim 37, wherein said cell line comprises at least ORF6 of the E4 region of the adenoviral genome.

F23. Vigne claim 1 reads:

1. A recombinant cell line for the production of a defective adenovirus comprising, inserted into its genome, part of an adenovirus E4 region comprising on ORF6 reading frame under the control of a functional promoter, wherein the inserted E4 region does not contain a functional ORF4 reading frame.

F24. Perricaudet claim 22 reads (see F15 for claim 19):

22. The cell line according to claim 19, wherein it comprises, in its genome, an E1 gene and an E4 gene wherein the E4 gene is under the control of an inducible promoter.

F25. Count 5 is defined by Kovesdi claim 59 or Kovesdi claim 74 or Perricaudet claim 42.

F26. Kovesdi claim 59 reads:

59. An adenoviral vector that requires, for replication, complementation *in trans* of one or more essential gene functions of each of at least the E2A and E4 regions of the adenoviral genome, which vector has been prepared using the cell line of claim 43.

F27. Kovesdi claim 74 reads:

74. The adenoviral vector of claim 68, wherein said vector is deficient in one or more essential gene functions in at least the E2A and E4 regions of the adenoviral genome.

F28. Perricaudet claim 42 reads:

42. A replication-defective adenovirus comprising an adenoviral genome that requires, for replication, complementation *in trans* of an essential gene function in each of at least two or more adenoviral early regions selected from the group consisting of the E1, E2A, and E4 regions

of an adenoviral genome,

wherein the adenovirus comprises one or more functional early or late gene regions of an adenoviral genome and requires complementation of an essential gene function in each of at least the E2A and E4 regions,

wherein the adenovirus comprises a heterologous DNA sequence.

F29. Count 6 is defined by Kovesdi claim 43 or Perricaudet claim 24.

F30. Kovesdi claim 43 reads (see F14 for Kovesdi claim 36):

43. The cell line of claim 36, wherein said vector is deficient in one or more essential gene functions of at least the E2A and E4 regions of the adenoviral genome.

F31. Perricaudet claim 24 reads (see F15 for claim 19):

24. The cell line according to claim 19, wherein it comprises E2 and E4 genes and the E2 and E4 genes are under the control of an inducible promoter.

F32. The claims of the parties are:

Kovesdi	19-26, 36-87, 89-95
Vigne	1-33
Perricaudet	1-3, 6, 9-30, 33-42

F33. The claims of the parties which correspond to Count 1 are:

Kovesdi	20-21, 24-26, 52, 56-58, 68-69, 72-73, 78-79, 84-87
Vigne	None
Perricaudet	1-3, 9, 12-18, 28, 30, 35, 40-41

F34. The claims of the parties which correspond to Count 2 are:

Kovesdi	19, 36, 41-42, 89-90, 95
Vigne	None
Perricaudet	19-20, 23, 25-27

F35. The claims of the parties which correspond to Count 3 are:

Kovesdi	20-21, 24-26, 52-56, 68-71, 78-79, 82, 84-87
Vigne	33
Perricaudet	1-3, 9, 12-18, 28, 30, 34, 40-41

F36. The claims of the parties which correspond to Count 4 are:

Kovesdi	19, 36-40, 89-90, 92-95
Vigne	1-6, 11-16, 20-21, 23-25
Perricaudet	19-23, 25, 27, 33

F37. The claims of the parties which correspond to Count 5 are:

Kovesdi	20-21, 24-26, 52-87
Vigne	None
Perricaudet	42

F38. The claims of the parties which correspond to Count 6 are:

Kovesdi	19, 36-41, 43-51, 89-90, 92-95
Vigne	None
Perricaudet	24

F39. The claims of the parties which do not correspond to any of Counts 1 through 6, and therefore are not involved in the interference, are:

Kovesdi	22-23, 91
Vigne	7-10, 17-19, 22, 26-32
Perricaudet	6, 10-11, 29, 36-39

Other findings of fact follow below.

III. Gencell Preliminary Motion 1

A. Relief requested is actually three motions in one

The opening paragraph of Gencell preliminary motion 1 reads:

> Pursuant to 37 C.F.R. § 1.633(c), Senior Party Gencell S.A. ("Gencell") moves to redefine the interfering subject matter by amending the claims of U.S. Patent Application 08/397,225 ("Perricaudet '225") as set forth in the Proposed Amendment attached hereto as Exhibit A and upon entry of the Proposed Amendment, substituting Proposed Count 1 for Count 1, Proposed Count 3 for Count 3, Proposed Count 4 for Count 4 and Proposed Count 6 for Count 6. The parties have conferred and Party Kovesdi indicated that this motion will be unopposed. [Paper 57, p. 2.]

According to Gencell, Perricaudet claim 1 is directed, in the alternative, to two

separately patentable species of recombinant replication-deficient adenoviruses. The first species is an adenovirus wherein E1 and E2 genes have been rendered non-functional, but E4 genes have not ("ΔE1,ΔE2"). The second species is an adenovirus wherein E1 and E4 genes have been rendered nonfunctional, but E2 genes have not ("ΔE1,ΔE4"). Therefore, Gencell proposes to amend Perricaudet claim 1 to limit it to the first species ΔE1,ΔE2 and to add new claim 43 directed to the second species ΔE1,ΔE4. Gencell further proposes to add new claims 44-64, dependent upon claim 43,[9] as "substantially identical copies of claims that currently depend from Claim 1." [Paper 57, p. 9.] Further according to Gencell, "[t]he Proposed Counts are necessitated by the proposed amendment to the Perricaudet application" (Paper 57, p. 10). Still further according to Gencell, "there is no interference-in-fact between the subject matter of Perricaudet '225 Claim 35 and Kovesdi '416 Claims" (Paper 57, p. 11).

Thus, Gencell preliminary motion 1 is actually three motions in one.

First, Gencell moves to redefine the interfering subject matter under 37 CFR § 1.633(c)(2) by amending Perricaudet **claims 1 and 2** which correspond to Counts 1 and 3 **as well as amending claim 11 which does not correspond** to any of Counts 1-6 and by adding proposed new claims 43 through 64 **which are not designated as corresponding to any of Counts 1-6**.

Second, Gencell moves to redefine the interfering subject matter under 37 CFR § 1.633(c)(1) by substituting proposed counts 1, 3, 4 and 6 for present Counts 1, 3, 4 and 6, respectively.

---

[9] Proposed new Perricaudet claim 64 is an independent claim. It does not depend from claim 43.

Third, Gencell argues **that there is no interference-in-fact** between Perricaudet claim 35 and Kovesdi's claims, a Rule 633(b) motion.

B. STANDING ORDER § 26

As stated in relevant part in § 26 of the STANDING ORDER (Paper 2),

> A party filing a motion has the burden of proof. 37 CFR § 1.637(a). In addition to complying with any procedural requirements of the rules and the STANDING ORDER, when a substantive issue is raised by a motion, a party bears a burden to establish its right to any substantive relief requested in the motion. See Hillman v. Shyamala, 55 USPQ2d 1220, 1221-22 (Bd. Pat. App. & Int. 2000). A motion which fails to comply with applicable procedural requirements may be dismissed without reaching the merits, in which case the issue sought to be raised by the motion is deemed not to have been properly presented for decision by the board. A motion which, while complying with applicable procedural requirements, nevertheless fails to make out a substantive case may be denied on the merits.

C. Rule 633(c)(2) motion - Proposed Amendment (Paper 57, pp. 9-10)

First, Rule 633(c)(2) does not provide for amending a claim or adding a claim which does not correspond to a count.

Second, according to 37 CFR § 1.637(c)(2)(iii), the movant must "show the patentability" to the applicant of each claim proposed to be amended or added.

A notice of the Chief Administrative Patent Judge addresses the issue of how one should interpret rules that require a Party to "show the patentability" of a claim in 1217 Off. Gaz. Pat. & Tm. Office 17-18 (December 1, 1998). The notice explains:

> The requirement of the rules that a party "show the patentability" of a claim may have led to some confusion as to precisely what is required to comply with the rules. This notice provides guidance with respect to the requirement to "show the patentability."
>
> The requirement that a party "show the patentability" of a claim should not be construed as requiring a party to prove a negative, i.e., that

there is no prior art which would anticipate the claim under 35 U.S.C. § 102 or render the claims unpatentable under 35 U.S.C. § 103. In this respect, the burden of establishing that a claim is not patentable generally falls on the party or individual alleging unpatentability. See e.g., 35 U.S.C. § 102 which provides that an applicant is "entitled to a patent unless * * *." See also Horton v. Stevens, 7 USPQ2d 1245, 1246-47 (Bd. Pat. App. & Int. 1988). Consistent with 37 CFR § 1.601, which provides that the rules should be construed to secure the just, speedy and inexpensive determination of interferences, the rules requiring a party to "show the patentability" of a claim normally should be interpreted as requiring that a party establish that the subject matter of the claim is described in the specification in the manner required by the first paragraph of 35 U.S.C. § 112. See also 37 CFR § 1.75(d)(1). The requirement can most effectively be met by reproducing the claim, and following each element recited in the claim, and within braces {} and in bold, insert a specific reference to the column and line and/or drawing figure and numeral where the element is described in the specification.

An exception would be a situation where a party files a preliminary motion under 37 CFR § 1.633(i) in response to an opponent's preliminary motion under 37 CFR § 1.633(a) for judgment. Since the party knows the basis for the opponent's preliminary motion for judgment, the party should also "show the patentability" of the claims proposed to be added by the preliminary motion under 37 CFR § 1.633(i) vis-a-vis the opponent's basis in the preliminary motion under 37 CFR § 1.633(a). Compare 37 CFR §§ 1.111(c) and 1.119 [(1998)].

The precise basis upon which a party is required to "show the patentability" necessarily will vary on a case-by-case basis.

Gencell has not met the requirements of 37 CFR § 1.637(c)(2)(iii).

Rather, Gencell argues that "Claim 1 of the Perricaudet '225 application was found allowable over the applicable prior art. [EX 1001, pg. 2]" (Paper 57, p. 6, #7 and p. 9). Gencell further argues that since amended claim 1 and proposed new claim 43 are each narrower than "original" claim 1, each is also separately patentable over the art of record (Paper 57, pp. 9-10). Gencell still further argues that new claims 56 and 64 "is allowable for at least the same reasons that claim 22 was allowed" (Paper 57, p.

7, #18, p. 8, #21 and p. 10).

This argument fails for three reasons: (i) it does not address the requirements of 37 CFR § 1.637(c)(2)(iii) as discussed above, (ii) "allowed" Perricaudet '225 claim 1 is not identical to pending claim 1[10] and (iii) decisions of a primary examiner during ex parte prosecution are not binding on the Board of Patent Appeals and Interferences in inter partes proceedings (Sze v. Bloch, 458 F.2d 137, 173 USPQ 498 (CCPA 1972); Okada v. Hitotsumachi, 16 USPQ2d 1789 (Comm'r. Pat. 1990); Glaxo Wellcome, Inc. v. Cabilly, 56 USPQ2d 1983 (Bd. Pat. App. & Int. 2000)).

Third, Gencell has not correlated each element recited in each amended and added claim with specific reference to column and line and/or drawing figure and numeral in Perricaudet '225 to show where each element is described. See also paragraph 21 of the STANDING ORDER (Paper 2) which requires specifying reference to page and line of specification and/or figure and item number of drawing within braces when a new claim is presented.

Fourth, according to 37 CFR § 1.637(c)(2)(ii), the movant must show that the claim proposed to be amended or added defines the same patentable invention as the count. As stated in 37 CFR § 1.601(n), invention "A" is the same patentable invention as invention "B" when "A" is the same as (35 U.S.C. § 102) or is obvious (35 U.S.C. § 103) in view of invention "B" assuming invention "B" is prior art with respect to invention

---

[10] Ex 1001 is identified as "Office Action in Perricaudet '225 application, dated July 22, 1996 (Paper 57, p. 5). Ex 1001 is responsive to an amendment filed May 8, 1996 (Ex 1001, pp. 1-2). A copy of the "**RESPONSE AND AMENDMENT UNDER 37 CFR § 1.111**" filed May 8, 1996 is attached to this decision as Ex 1500. Claims 1, 2 and 11, e.g., pending in Perricaudet '225 as of the entered May 8, 1996 amendment (see Ex 1500) are not identical to the currently pending Perricaudet claims.

"A." Gencell has not shown that amended claims 1, 2 and 11 and added claims 43-64 are anticipated by or obvious over any claims corresponding to any of Counts 1-6.

Therefore, entry of the proposed amended and added claims is denied for non-compliance with the requirements of Rule 637(c)(2)(ii) and (iii) and paragraph 21 of the STANDING ORDER.

D. Rule 633(c)(1) motion - Proposed Counts (Paper 57, pp. 10-17)

Fifth, according to 37 CFR § 1.637(c)(1)(ii), the movant must "show the patentability" to the applicant of all claims in or proposed to be added to, the party's application which correspond to each proposed count and apply the terms of the claims to the disclosure of the party's application.

Gencell has not met the requirements of 37 CFR § 1.637(c)(1)(ii) for the reasons given above.

E. Rule 633(b) motion - For no interference-in-fact between Perricaudet claim 35 and Kovesdi's claims

Nitz v. Ehrenreich, 537 F.2d 539, 544, 190 USPQ 413, 417 (CCPA 1976) stated that

> [t]he materiality of a limitation is directly related to its significance within the invention as a whole. Cf. In re Frilette, 58 CCPA 799, 436 F.2d 496, 168 USPQ 368 (1971). In McCabe v. Cramblet, supra, which we quoted with favor in Brailsford v. Lavet, supra, this court stated:
>
> > The first question for consideration is whether there is any patentable distinction between the counts here involved and said claims 1 to 5 of appellant's patent; or, in other words, do the claims of said patent and the counts of the interference call for the same invention? ... the test is whether the counts of the interference and the claims of the patent call for the same invention. ...

Thus, Gencell can establish that no interference-in-fact exists as to Perricaudet

claim 35 by showing that Perricaudet claim 35 is not anticipated or rendered obvious by any of the involved Kovesdi claims corresponding to Count 1 (the only count to which Perricaudet claim 35 corresponds) or vice versa. That is, no interference-in-fact is subject to a "one-way" test for patentable distinctiveness.

Gencell argues

> ...there is no interference-in-fact between the subject matter of Perricaudet '225 Claim 35 and Kovesdi '416 Claims. In this regard, the adenovirus of Perricaudet '225 Claim 35 wherein the E4 early region is the sole adenoviral region is patentably distinct from the adenoviruses of Kovesdi claims 57 and 72 which contain deletions of genes in the E1 and E2A early regions and possible deletion in the E4 early gene region. From the perspective of Kovesdi Claim 52, an adenovirus wherein genes in two early regions selected from E1, E2A and E4 regions are deleted is patentably distinct from an adenovirus having all of the E1, E2 and E3 regions deleted, as required by Perricaudet claim 35. ... [Paper 57, p. 11]

However, Gencell's argument is both incomplete and insufficient. Gencell has not established either that Perricaudet claim 35 is not anticipated by or rendered obvious over any of Kovesdi claims 20-21, 24-26, 52, 56-58, 68-69, 72-73, 78-79 and 84-87 (which correspond to Count 1) or vice versa. Kovesdi claim 69, for example, encompasses further deletion of E3. Clearly, the more of the adenoviral genome that is deleted from an adenoviral vector, the more transgene that can be inserted into the vector. An unsupported "perspective" is insufficient to satisfy Gencell's burden of proof as movant.

F. Motion is dismissed

Thus, for the above reasons, Gencell preliminary motion 1 is **dismissed** without prejudice to the APJ taking further appropriate action.

IV. Gencell Preliminary Motion 2

Gencell moves under 37 CFR § 1.633(f) [and (j)] to be accorded benefit for the purpose of priority of the filing dates of Gencell (i) PCT application PCT/FR94/00851, filed July 8, 1994, (ii) FR application 94/04590, filed April 18, 1994 and (iii) FR application 93/08596, filed July 13, 1993, for the subject matter of Proposed Count 1 (Paper 58). Gencell preliminary motion 2 is contingent upon the grant of Gencell preliminary motion 1. Gencell preliminary motion 1 has been dismissed without prejudice to the APJ taking further appropriate action as discussed above. Therefore, Gencell preliminary motion 2 is moot.

Gencell preliminary motion 2 is **dismissed** as moot.

V. Gencell Preliminary Motion 3

Gencell moves under 37 CFR § 1.633(f) [and (j)] to be accorded benefit for the purpose of priority of the filing dates of Gencell (i) PCT application PCT/FR94/00851, filed July 8, 1994, (ii) FR application 94/04590, filed April 18, 1994 and (iii) FR application 93/08596, filed July 13, 1993, for the subject matter of Proposed Count 3 (Paper 59). Gencell preliminary motion 3 is contingent upon the grant of Gencell preliminary motion 1. Gencell preliminary motion 1 has been dismissed without prejudice to the APJ taking further appropriate action as discussed above. Therefore, Gencell preliminary motion 3 is moot.

Gencell preliminary motion 3 is **dismissed** as moot.

VI. Gencell Preliminary Motion 4

Gencell moves under 37 CFR § 1.633(f) [and (j)] to be accorded benefit for the

purpose of priority of the filing dates of Gencell (i) PCT application PCT/FR94/00851, filed July 8, 1994, (ii) FR application 94/04590, filed April 18, 1994 and (iii) FR application 93/08596, filed July 13, 1993, for the subject matter of Proposed Count 4 (Paper 60). Gencell preliminary motion 4 is contingent upon the grant of Gencell preliminary motion 1. Gencell preliminary motion 1 has been dismissed without prejudice to the APJ taking further appropriate action as discussed above. Therefore, Gencell preliminary motion 4 is moot.

Gencell preliminary motion 4 is **dismissed** as moot.

V. Gencell Preliminary Motion 5

Gencell moves under 37 CFR § 1.633(f) [and (j)] to be accorded benefit for the purpose of priority of the filing dates of Gencell (i) PCT application PCT/FR94/00851, filed July 8, 1994, (ii) FR application 94/04590, filed April 18, 1994 and (iii) FR application 93/08596, filed July 13, 1993, for the subject matter of Proposed Count 6 (Paper 61). Gencell preliminary motion 5 is contingent upon the grant of Gencell preliminary motion 1. Gencell preliminary motion 1 has been dismissed without prejudice to the APJ taking further appropriate action as discussed above. Therefore, Gencell preliminary motion 5 is moot.

Gencell preliminary motion 5 is **dismissed** as moot.

VI. Gencell and Kovesdi Joint Preliminary Motion 1

The parties jointly move pursuant to 37 CFR § 1.633(c)(4) for judgment that Kovesdi claims 39, 45, 48, 51 and 94, currently designated as corresponding to Counts 4 and 6, do not correspond to any of Counts 1-6. The parties further jointly move

pursuant to 37 CFR § 1.633(c)(1) to redefine the interfering subject matter by adding a Proposed Count 7 and designating Kovesdi claims 39, 45, 48, 51 and 94 and Vigne/Gencell claim 19 as corresponding to Proposed Count 7. [Paper 67]

F40. Kovesdi claims 39, 45, 48, 51 and 94 are drawn to complementing cell lines, derived from HEK 293 or A549 cells, for replication defective adenoviral vectors wherein one or more essential gene functions of each of two or more regions adenoviral early gene regions selected from the group consisting of E1, E2A and E4 are nonfunctional, *wherein said cell line comprises ORF6 and no other ORF of the E4 region of the adenoviral genome* (Kovesdi claims 39, 45, 48 and 51) or *wherein said cell line comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome* (Kovesdi claim 94).

A. Technical background

F41. It was known by at least 1983 that 293 cells, a line of human embryonic kidney cells transformed by sheared adenoviral DNA, supported the growth of E1 deletion mutant adenoviruses (Ex 3005,[10] p. 5383, ¶ 1 and Ex 3004[11]).

F42. It was also known by 1983 that the W162 cell line, which contains an intact adenoviral E4 region, supported the growth of an E4 deletion adenovirus mutant (Ex 3005).

F43. There are seven known open reading frames in the E4 region, i.e., ORF1,

---

[10] David H. Weinberg and Gary Ketner, "A cell line that supports the growth of a defective early region 4 deletion mutant of human adenovirus type 2," Proceedings of the National Academy of Sciences: USA, Vol. 80, pp. 5383-5386 (September 1983).

[11] Graham et al., "Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5," Journal of General Virology, Vol. 36, pp. 59-74 (1977).

ORF2, ORF3, ORF4, ORF3/4, ORF6 and ORF6/7 (Ex 3002,[12] Figure 1a; Ex 3003,[13] p. 631, c. 1, ¶ 2).

F44. In 1987 Cutt,[14] whose study focused on the products encoded by E4 ORFs 6 and 7, reported that

> [t]he 6/7 fusion polypeptides may be functionally, as well as structurally, related to the ORF 6 34K protein. ... Deletion of E4 ORFs 1 through 4 has no effect on virus viability in lytic infection of HeLa cells .... Mutant *dl*355 (ORF 6 deletion) is moderately defective for lytic growth, and *dl*366 (deletion of all E4 ORFs) is severe defective for viral growth.... Since **ORFs 1 through 4 are dispensible for virus growth**, the difference in the severities of the *dl*355 and *dl*366 phenotypes may be due to the presence (*dl*355) or absence (*dl*366) of the ORF 6/7 fusion products within infected cells. We speculate that the ORF 6 34K and ORF6/7 fusion polypeptides are functionally related and that the 6/7 fusion products allow *dl*355 to grow significantly better than *dl*366 in lytic infection. ... Thus, **the essential E4 sequences required for virus viability in lytic infection may reside solely within the amino terminus of ORF6**. .... [Ex 3012, ¶ bridging pp. 550-551, emphasis added.]

F45. In 1989, Bridge I reported

> ...(i) that the products of ORF 6 and ORF 3 can individually provide an E4 function that results in nearly normal late protein synthesis, (ii) that the E4-related protein synthetic defect is observed independently of a defect in DNA accumulation, and (iii) that although optimal plaque formation on noncomplementing cell lines requires the ORF 6 product, the ORF 3 product suffices for plaquing at a slightly lower efficiency (Ex 3003, p. 631, c. 2, ¶ 1).

In other words, "either ORF6 or ORF3 can individually provide a function that permits

---

[12] Gary Ketner, Eileen Bridge, Anders Virtajnen, Catherine Hemstrom and Ulf Pettersson, "Complementation of adenovirus E4 mutants by transient expression of E4 cDNA and deletion plasmids," Nucleic Acids Research, Vol. 17, No. 8, pp. 3037-3048 (1989).

[13] Eileen Bridge and Gary Ketner (Bridge I), "Redundant Control of Adenovirus Late Gene Expression of Early Region 4," Journal of Virology, Vol. 63, No. 2, pp. 631-638 (February 1989) (Ex 3003).

[14] Cutt et al. (Cutt), "Analysis of Adenovirus Early Region 4-Encoded Polypeptides Synthesized in Productively Infected Cells," Journal of Virology, Vol. 61, No. 2, pp. 543-552 (February 1987) (Ex 3012).

plaque formation, although ORF6 appears to be required for optimal plaquing ability"[15] (Ex 3003, p. 636, c. 2, ¶ 5).

F46. Also in 1989, Ketner (which included the authors of Bridge I) reported that "[p]lasmids carrying ORFs 1, 2, 3/4, 4, and 6/7 in the absence of ORFs 3 and 6 are inactive in complementing E4 mutants" (Ex 3002, p. 3046, c. 1, ¶ 3).

F47. In 1993, Bridge II reported that "E4 products are not absolutely required for viral DNA replication" (Ex 3009, p. 794, c. 2, ¶ 2).[16] According to Bridge II, "[t]he removal of all E4 products from an infected cell by mutation would result in unregulated DNA synthesis, which in HeLa cell monolayers happens to permit the accumulation of viral DNA in an amount only slightly different from that produced by normally regulated synthesis" (id., p. 799, c. 2, ¶ 2). Bridge II proposed that the ORF 4 product acts to down-regulate viral DNA synthesis, while the ORF 3 (3/4) and ORF 6 products act either to moderate the effect of the ORF 4 product or to stimulate DNA replication by another mechanism (id.).

Bridge II is not inconsistent with the opening paragraph in Bridge I, i.e.,

> The adenovirus infectious cycle includes two programs of gene expression, early and late, which are characterized by the expression of

---

[15] The plaque method is used to detect and count viruses. A mixture of virus, host cell and agar is poured into a Petri plate containing a hardened layer of agar growth medium to form a top monolayer of host cells. Each virus infects a host cell, multiplies and releases several hundred new viruses. The newly produced viruses infect adjacent host cells and more viruses are produced. After several viral multiplication cycles, all the host cells in the area surrounding the original virus are destroyed or lysed. This produces a number of clearings or "plaques" on the surface of the agar against a "lawn" or turbid background of uninfected host cells. See MICROBIOLOGY: An Introduction, by Tortora et al., pp. 321-22 (The Benjamin/Cummings Publishing Company, Inc., Menlo Park California) (1982) (copy attached).

[16] Eileen Bridge, Susan Medghalchi, Sukithida Ubol, Minsun Leesong, and Gary Ketner (Bridge II), "Adenovirus Early Region 4 and Viral DNA Synthesis," Virology, Vol. 193, pp. 794-801 (1993) (Ex 3009).

> different sets of viral genes and are separated by the onset of DNA replication. Expression of early region genes is necessary for normal progression from the early to the late program. In particular, the analysis of two large deletion mutants of early region 4 (E4) ... has implicated E4 in many of the events that occur as the late program begins; the mutants have complex phenotypes that include defects in late protein synthesis, late mRNA accumulation, DNA accumulation, and shutoff of host cell protein synthesis. ... [Ex 3003, endnotes omitted.]

nor with the statement in Bridge I "that the effect on late protein synthesis of E4 mutations is not simply the result of a failure of cells infected by E4 mutants to accumulate normal amounts of viral DNA" (Ex 3003, p. 636, c. 1, ¶ 3).

Thus, based on the foregoing, one of ordinary skill in the art would have had a reasonable basis for believing that E4 ORF6, in the absence of other E4 ORFs, would have been sufficient to complement E4 adenoviral mutants, although apparently the exact mechanism(s) by which complementation occurred was unknown.

B. Rule 637(c)(4)(ii)

Rule 637(c)(4)(ii) requires a movant seeking to designate an application or patent claim as not corresponding to a count to show that the claim does not define the same patentable invention as any other claim whose designation in the notice declaring interference as corresponding to the count the party does not dispute.

Here, parties Gencell and Kovesdi contend that Kovesdi claims 39, 45, 48, 51 and 94 do not define the same patentable invention as claims designated as corresponding to Counts 4 and 6, i.e., Kovesdi claims 19, 36-38, 40, 41, 43, 44, 46, 47, 49, 50, 89, 90, 92, 93 and 95; Vigne claims 1-6, 11-16, 20, 21 and 23-25; and, Perricaudet claims 19-25, 27 and 33 (Paper 67, ¶ bridging pp. 12-13).

C. The parties joint position

The parties contend that, at the time the Perricaudet '225 and Kovesdi '416 applications were filed,

> ...one of ordinary skill in the art was not aware that the protein encoded by E4 ORF6 is the only E4 product necessary for growth of an adenoviral vector deleted of the entire E4 region in a non-E4 complementing cell line. Moreover, one of ordinary skill in the art was not aware that a cell line with ORF6 and no other ORF of the E4 region could propagate an adenoviral vector with deficiencies in replication-essential gene functions of the E4 region as well as either or both of the E1 region and the E2A region, let alone that such a cell line would be superior to cell lines with ORF6 and other ORFs of the E4 region. While it was known that the E4 region contained seven ORFs, it was not known with any reasonable degree of certainty at that time which of these E4 ORFs are required to support adenoviral growth in a complementary cell line, particularly in the context of propagating an adenoviral vector with deficiencies in replication-essential gene functions of the E4 region as well as either or both of the E1 region and the E2A region. [Paper 67, ¶ bridging pp. 17-18, citations to the parties statements of material facts omitted.]

D. Analysis of claim correspondence

1. Kovesdi claims 39, 45, 48, 51 and 94 are obvious over the Gencell claims corresponding to Counts 4 and 6 in view of Cutt, Ketner, Bridge I and Bridge II

First, Kovesdi claims 39, 45, 48, 51 and 94 are not anticipated by the other claims designated as corresponding to Count 4 or 6 because none of the other claims include the limitation that the complementing cell line "comprise ORF6 and no other ORF of the E4 region of the adenoviral genome."

However, it would have been prima facie obvious to modify the cell line of the other corresponding claims, e.g., Vigne claim 12 or Perricaudet claim 24, 27 or 33,[17]

---

[17] Vigne claim 12 recites a recombinant cell line derived from cell line 293, which transcomplements for the E1 and E4 adenoviral regions, having a part of an adenovirus E4 region

which can contain E4 ORF6 as well as other ORFs of the E4 region in its genome, by inserting an adenoviral E4 region containing ORF6 and no other E4 ORF into its genome because ORF 6 encodes the only E4 product necessary for growth of an adenoviral vector deleted of the entire E4 region as disclosed by Cutt (Ex 3012), Ketner (Ex 3002), Bridge I (Ex 3003) and Bridge II (Ex 3009), and because such a modification would also be expected to avoid down-regulation of DNA viral synthesis by the product of the E4 ORF4 as suggested by Bridge I and II. See § VI. A. above.

2. The evidence is insufficient to establish unexpected results

A conclusion of prima facie obviousness, of course, does not end a patentability analysis. As stated in In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988):

> There is always a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious.

The parties argue that a cell line comprising E4 ORF6 and no other E4 ORF, e.g., the 293/ORF6 cell line described in Kovesdi '416 Example 9, is surprisingly much more efficient in propagating E1/E4-deficient adenoviral vectors than a cell line comprising E4 ORF6 and other ORFs of the E4 region, e.g., the 293/E4 cell line described in Kovesdi '416 Example 8 (Paper 67, p. 19). The parties further argue that "the 293/ORF6 cell line has a substantially reduced probability of producing an

---

inserted into its genome, wherein the inserted E4 region comprises an ORF6 but not a functional ORF4. Perricaudet claim 19 recites a cell line capable of complementing an adenovirus wherein E1 genes have been rendered non-functional by deletion and wherein either E2 or E4 genes, but not both, have been rendered non-functional by deletion. Perricaudet claims 27 and 33 require the cell line of claim 19 to be derived from a 293 cell line and to comprise E4 ORFs 6 and 6/7, respectively. Perricaudet claim 24 requires the cell line of claim 19 to comprise both E2 and E4 genes.

undesired replication-competent adenoviral vector (RCA) through homologous recombination with shared sequences between the complementing cell and an adenoviral vector propagated in the complementing cell" (Paper 67, p. 19).

F48. Kovesdi '416 Example 8 is said to describe the preparation of a 293/E4 cell line which is said to be capable of complementing adenoviral vectors defective in both E1 and E4 functions, such as Ad_{GV}CFTR.12 (Ex 3001, pp. 28-30).

F49. Similarly, Kovesdi '416 Example 9 is said to describe the preparation of a 293/ORF6 cell line which is said to be capable of complementing adenoviral vectors deficient in the E1 and E4 functions, such as Ad_{GV}CFTR.12 (Ex 3001, p. 30).

The parties have not pointed us to, and we do not find, where Kovesdi '416 describes any comparative data between the 293/E4 and 293/ORF6 cell lines.

Although Kovesdi '416 identifies recombination events resulting in creation of RCA as a problem when using singly deficient adenoviral vectors in gene therapy (Ex 3001, ¶ bridging pp. 8-9), the parties have not pointed us to, and we do not find, where Kovesdi '416 describes any scientific data relating to the incidence of recombination events resulting in RCA when using multiply deficient adenoviral vectors.

F50. Douglas E. Brough, Ph.D., one of the Kovesdi inventors, testified that the 293/E4 and 293/ORF6 cell lines described in Examples 8 and 9 of Kovesdi '416 were subjected to standard virology analysis as described in his laboratory notebook (Exs 3018-3020) and in published work from his laboratory (Ex 3017) (Paper 72, Ex 3006, ¶¶ 6 and 7).

F51. David A. Ornelles, Ph.D., testified for the parties that he understood "that

the 293/E4 cell line and 293/ORF6 cell lines described in Examples 8 and 9 of Kovesdi '416 were subjected to standard virology analysis as described in Exs 3017-3020 (Paper 71, Ex 3007, ¶¶ 5 and 6).

F52. Both declarants identified Exs 3001 and 3017-3020 as

Exhibit 3001 - U.S. Patent Application 08/258,416 ("the Kovesdi '416 application)"

Exhibit 3017 - Brough et al., *J. Virol.* 70(9), 6497-6501 (1996)

Exhibit 3018 - Laboratory Notebook No. 6 of Douglas E. Brough, Ph.D., pp. 39-40

Exhibit 3019 - Laboratory Notebook No. 6 of Douglas E. Brough, Ph.D., p. 116

Exhibit 3020 - Laboratory Notebook No. 6 of Douglas E. Brough, Ph.D., pp. 140-141

(Paper 71, Ex 3007, ¶ 2; Paper 72, Ex 3006, ¶¶ 2 and 7).

F53. Drs. Brough and Ornelles both testified that "in combining the feature of complementing for an E1-deficiency with the feature of complementing for an E4 deficiency, the 293/E4 cell line does not complement for either an E1-deficiency or an E4-deficiency as well as the 293 cell line or the W162 cell line, respectively, as measured by virus production levels (EXHIBIT 3019, page 116; EXHIBIT 3018, page 40)" (Paper 72, Ex 3006, ¶ 8 and Paper 71, Ex 3007, ¶ 7).

Section 43 of the STANDING ORDER states, in relevant part,

> In the event a party relies on a scientific test or data generated from a scientific test, the party relying on the test or data shall explain:
> (a) the reason why the test is being used and why the data is being relied upon;
> (b) how the test is performed;
> (c) how the data is generated using the test;
> (d) how the data is used to determine a value;
> (e) the acknowledged accuracy of the test; and
> (f) any other information which would aid the board in understanding the significance of the test or data.

> Any explanation should take place through affidavit testimony of a witness, preferably accompanied by citation to relevant pages of standard texts (which should be exhibits in the interference).

Neither Dr. Brough nor Dr. Ornelles has explained the data in Exs 3018 and 3019 in compliance with § 42 of the STANDING ORDER. Not only are several of the handwritten entries in Exs 3018 and 3019 impossible to read, but also several of the readable entries raise a question about the accuracy and reliability of the data.

Exhibit 3018 appears to contain a notation that the number of cells per dish was not accurately controlled and, therefore, the pfu/cell could not be reported reliably (p. 40, ll. 47-7). If the data is not statistically accurate, it is unclear how results could be credibly compared. Exhibit 3018, p. 40 also appears to reference some sort of "lag in virus production" (fourth line from bottom). This raises questions as to timing. Bridge II reported that "at higher multiplicities (25 to 50 plaque-forming units per cell) and late times after infection (24 hr), most E4 mutants accumulate viral DNA in amounts comparable to those found in cells infected by wild-type virus" (Ex 3009, p. 794, c. 2, ¶ 2). Since dl366 is an E4 mutant, it may be that either multiplicity of infection or time after infection is affecting the data in Exhibit 3018. Moreover, Exhibit 3018, p. 40 ends with the word "retest."

Furthermore, Exhibit 3018 appears to describe growing an E4-deficient adenoviral vector (dl366) in three different cell lines, i.e., an E4-complementing cell line (W162), an E1-complementing cell line (293) and an E1/E4-complementing cell line

(clone #25).[19] It seems that dl366 not only grew in cell lines W162 and clone #25 (which would have been expected to supply dl366's missing E4 function), but also in the 293 cell line. It is unclear how an E1-complementing cell line would supply a missing E4 gene function.

Moreover, it appears that zinc chloride ($ZnCl_2$) was added in amounts of 0, 10 and 100 µM. It is unclear how added zinc chloride affects the data. Finally, it is unclear whether the results of "clone #25" are representative of the "293/E4" genus of complementing cell lines.

Therefore, Exhibit 3018 appears to be of little probative value.

The data in Exhibit 3019 is similarly unexplained. Further, there is the question of the presence (and amount) of zinc chloride again. Moreover, it appears that the E4-deficient dl366 failed to grow in any of four 293/E4 complementing cell lines (#12, #23, #25 and #55). Yet, according to Exhibit 3018, dl366 grew in 293/E4 cell line #25.

Therefore, Exhibit 3019 also appears to be of little probative value.

F54. Drs. Brough and Ornelles both further testified that "[d]espite the fact that the 293/ORF6 cell line comprises only a small portion of the E4 region ... the 293/ORF6 cell line nevertheless can propagate E1/E4-deficient adenoviral vectors (EXHIBIT 3017, page 6947, column 2, first complete paragraph)" (Paper 72, Ex 3006, ¶ 9 and Paper 71, Ex 3007, ¶ 8).

---

[19] Drs. Brough and Ornelles identified the materials used as "the 293 cell line (an E1-complementing cell line), the W162 cell line (an E4-complementing cell line), the 293/E4 cell line (an E1/E4-complementing cell line), the 293/ORF6 cell line (an E1/E4 complementing cell line), dl366 (an E4-deficient adenoviral vector), dl312 (an E1-deficient adenoviral vector), AdGVCFTR.10 (an E1-deficient adenoviral vector), AdRSVßgal.11 (an E1/E4-deficient adenoviral vector), and AdCFTR.11A (an E1/E4-deficient adenoviral vector)" (Paper 72, Ex 3006, ¶ 7; Paper 71, Ex 3007, ¶ 6).

However, as discussed in § VI A above, one of ordinary skill in the art would have had a reasonable basis for believing that E4 ORF6, in the absence of other E4 ORFs, would have been sufficient to complement E4 adenoviral mutants. Indeed, Exhibit 3017 itself states, "[o]f the possible open reading frame (ORF) products encoded by the E4 region, only one, either ORF3 or ORF6, is absolutely required for viral growth in tissue culture (2, 10, 13, 18)" (Ex 3017, p. 6497, c. 1, last sentence of ¶ 2). Of the four references cited to support this statement, two, i.e., 2 and 18, are the Bridge I (Ex 3003) and Ketner (Ex 3002) 1989 articles discussed above. Therefore, the ability of E4 OFR6 to provide the necessary replication function of the entire E4 gene region is not inconsistent with the state of the art.

F55. Drs. Brough and Ornelles still further both testified that "[s]trikingly [Dr. Brough]/surprisingly [Dr. Ornelles], and in contrast to the 293/E4 cell line described above, the 293/ORF6 cell line functions substantially as well as the 293 cell line in propagating E1-deficient adenoviral vectors, and it functions substantially as well as the W162 cell line in propagating E4-deficient adenoviral vectors, as measured by virus production levels (EXHIBIT 3020, page 141)" (Paper 72, Ex 3006, ¶ 9 and Paper 71, Ex 3007, ¶ 8).

The data in Ex 3020 is unexplained. For example, the graph depicted on page 141 appears to involve testing six different cell lines:

(1) the E4-complementing W162 cell line,
(2) the E1-complementing 293 cell line,
(3) a #216- clone of a 293/ORF6 E1/E4 complementing cell line in the absence of an unknown,
(4) a #216+ clone of a 293/ORF6 E1/E4 complementing cell line in the presence of an unknown,

(5) a #406- clone of a 293/ORF6 E1/E4 complementing cell line in the absence of an unknown, and
(6) a #406+ clone of a 293/ORF6 E1/E4 complementing cell line in the presence of an unknown.

The presence of the unknown appears to have affected the virus production of the #216 clone by about a factor of ten, but not to have affected the virus production of the #406 clone. Parameters such as multiplicity of infection, test time after infection, etc. are undefined.

Moreover, the relationship between the numerical data on p. 140 (Ex 3020) and the graph on p. 141 (Ex 3020) is unstated. Assuming arguendo that the #xxx designations referred to clones of 293/ORF6 cell lines, then the data on p. 140 might be grouped as follows:

	dl312 (E1-deficient vector)	AdGVCFTR.10 (E1-deficient vector)	dl366 (E4-deficient vector)
293 (E1+ cell)	1300.000	**565.000**	**0.875**
W162 (E4+ cell)	238.000	**0.010**	**2275.000**
#112 (E1+, E4+ cell)	550.000	90.000	1.000
#118 (E1+, E4+ cell)	1700.000	240.000	14.000
#120 (E1+, E4+ cell)	850.000	270.000	1.000
#202 (E1+, E4+ cell)	3150.000	650.000	1.000
#209 (E1+, E4+ cell)	850.000	900.000	1.000
#216 (E1+, E4+ cell)	900.000	**200.000**	**50.000**
#304 (E1+, E4+ cell)	1450.000	210.000	9.250
#406 (E1+, E4+ cell)	950.000	**290.000**	**292.000**
#408 (E1+, E4+ cell)	1090.000	850.000	1.000

We will not guess what significance this data compilation may or may not have.

Therefore, Exhibit 3020 appears to be of little probative value.

F55. Drs. Brough and Ornelles yet still further both testified that "[m]oreover, the 293/ORF6 cell line surprisingly is much more efficient than the 293/E4 cell line in propagating E1/E4-deficient adenoviral vectors" (Paper 72, Ex 3006, ¶ 9 and Paper 71, Ex 3007, ¶ 8).

Neither declarant points to any evidence of record to support this conclusion. Opinions expressed without disclosing the underlying facts or data may be given little, or no, weight. See Rohm and Hass Co. v. Brotech Corp., 127 F.3d 1089, 1092, 44 USPQ2d 1459, 1462 (Fed. Cir. 1997) (nothing in the Federal Rules of Evidence or Federal Circuit jurisprudence requires the fact finder to credit the unsupported assertions of an expert witness).

F56. Drs. Brough and Ornelles both declare that

> The 293/ORF6 cell line has other advantages over the 293/E4 cell line. The ability to complement for deficiencies in replication-essential gene functions in an adenoviral vector with a cell line comprising ORF6 and no other ORF of the E4 region, as exemplified by the 293/ORF6 cell line, greatly reduces the amount of viral products expressed by the cell line and reduces the probability of producing an undesired replication-competent adenoviral vector (RCA) through homologous recombination with shared sequences between the complementing cell and an adenoviral vector propagated in the complementing cell. Stocks of adenoviral vectors free from contaminating virus, such as RCA, are desired for controlled gene transfer to patients. [Paper 72, Ex 3006, ¶ 10 and Paper 71, Ex 3007, ¶ 9.]

First, if less than all of the E4 ORFs are introduced into the genome of a complementing cell, then it appears logical that the complementing cell line will produce fewer viral products, i.e., the products encoded by the missing E4 ORFs will not be produced. Second, production of undesired RCA as argued above is not solely dependent upon the complementing cell line. As stated in the Brough et al. article,

published more than two years after the June 10, 1994 filing date of Kovesdi '416, "Since no overlapping sequences between the new cell lines and the genome of the vector with E4 deleted exist, no generation of replication-competent virus by homologous recombination will occur" (Ex 3017, p. 6497, c. 2, ¶ 2). Nor have the parties pointed us to any evidence supporting a conclusion that any E4-deficient adenoviral vector can be propagated in a 293/ORF6 complementing cell line without generation of RCA. Thus, it appears to be a selected combination of complementing cell line and deletion adenoviral vector that is needed to avoid generation of RCA by homologous recombination.

Therefore, this argument, too, is insufficient to establish unexpected results of the 293/ORF6 cell line per se.

E. Addition of proposed Count 7 is moot

Party Kovesdi [and Gencell] move pursuant to 37 CFR § 1.633(c)(1) to add "Proposed Count 7" to the interference (Paper 67, pp. 1 and 20). Proposed Count 7 reads (Paper 67, p. 20):

> A cell line that complements in *trans* an adenoviral vector having an adenoviral genome, said genome being deficient in one or more essential gene functions of each of the E1 and E4 regions of said adenoviral genome, the cell line comprising ORF6 of the E4 region operably linked to an inducible or repressible promoter and comprising no other complete ORF of the E4 region.
>
> In the "McKelvey" format, the proposed Count 7 is:
> The cell line of claim 39 of the Kovesdi '416 application, or
> The cell line of claim 19 of the Vigne '175 patent.

Insofar as the parties have failed to satisfy their burden of establishing that the subject matter defined by Kovesdi claims 39, 45, 48, 51 and 94 defines a separately

patentable invention from the subject matter of Counts 4 and 6, for the reasons given above, the parties have also failed to satisfy their burden to show that proposed Count 7 defines a separately patentable invention from every other count proposed to remain in the interference. 37 CFR § 1.673(c)(1)(v).

Therefore, joint preliminary motion 1 is **denied**.

VII. Kovesdi Preliminary Motion 1

Kovesdi moves pursuant to 37 CFR § 1.633(c)(2) to amend Kovesdi claim 19 to delete one embodiment, i.e., a 293 cell line that is stably transfected with a pSMT/ORF-6 plasmid, contending that this is a separately patentable invention from the subject matter of Counts 4 and 6 (Paper 66). In other words, Kovesdi preliminary motion 1 is contingent upon the grant of joint preliminary motion 1. Joint preliminary motion 1 has been denied. Therefore, Kovesdi preliminary motion 1 is **dismissed** as moot.

VIII. Gencell and Kovesdi Joint Preliminary Motion 2

The parties jointly move pursuant to 37 CFR § 1.633(c)(3) to designate Vigne claims 17 and 18 and, if joint preliminary motion 1 is denied, also Vigne claim 19 as corresponding to Count 4 (Paper 68).

Vigne claims 17-19 are currently designated as not corresponding to any of Counts 1 through 6 (F39).

Count 4 is directed to recombinant cell lines comprising at least ORF6 of the E4 region of the adenoviral genome and is defined by Kovesdi claim 38 or Vigne claim 1 or Perricaudet claim 22 (F21-24).

Vigne claim 1 is directed to a recombinant cell line comprising, inserted into its

genome, a part of an adenovirus E4 region comprising an ORF6 under the control of a functional promoter, wherein the inserted E4 region does not contain a functional ORF4 (F23).

F57. Vigne claim 2, which corresponds to Count 4, reads:

> 2. The cell line according to Claim 1, wherein the E4 region further comprises a reading frame ORF6/7.

F58. Vigne claim 17 reads:

> 17. The cell line according to claim 1, wherein the part of the E4 region is a Bg1II-Bg1II fragment corresponding to nucleotides 34115-32490 of the Ad5 genome, or the corresponding nucleotides from Ad2, Ad7 or Ad12.

F59. Vigne claim 12 reads:

> 12. The cell line according to Claim 11, which is derived from cell line 293.

F60. Vigne claim 18 reads:

> 18. The cell line according to claim 17, which is a 293 line.

F61. Vigne claim 19 reads:

> 19. The cell line according to claim 1, wherein the part of the E4 region is a BG1II-PvuII fragment corresponding to nucleotides 34115-33126 of the Ad5 genome, or the corresponding nucleotides from Ad2, Ad7 or Ad12.

F62. Ad2 E4 ORF6 spans approximately nucleotides 34077 through 33195, while ORF6/7 spans approximately nucleotides 34077 through 32916 (Ex 1008, Table 1). Ad2 E4 ORF4 spans approximately nucleotides 34000 through 34342 (id.).

Thus, the BG1II-PvuIII fragment of Vigne claim 17 appears to contain the complete E4 ORF6 plus a flanking sequence on either side, but no other complete E4

ORF. Similarly, the BG1II-PvuII fragment of Vigne claim 19 appears to contain the complete E4 ORFs 6 and 6/7 plus a flanking sequence on either side, but no other complete E4 ORF.

To designate an application or patent claim as corresponding to a count, the claim must define the same patentable invention as any other claim whose designation as corresponding to the count is not disputed. 37 CFR § 1.637(c)(3)(ii).

The parties state that the invention defined by Vigne claims 19, 17 and 18 is the same invention as defined by Vigne claims 1, 2 and 12, which claims have been designated as corresponding to Count 4, and vice versa (Paper 68, pp. 6-7). This statement is not inconsistent with describing E4 regions either by ORF number or by restriction enzyme fragments containing only those complete E4 ORFs.

Therefore, joint motion 2 is **granted.**

IX. Order

Upon consideration of Gencell preliminary motion 1, and for the reasons given, it is

ORDERED that Gencell preliminary motion 1 is **dismissed** without prejudice to the APJ taking further appropriate action.

Upon consideration of Gencell preliminary motion 2, and for the reasons given, it is

ORDERED that Gencell preliminary motion 2 is **dismissed** as moot.

Upon consideration of Gencell preliminary motion 3, and for the reasons given, it is

ORDERED that Gencell preliminary motion 3 is **dismissed** as moot.

Upon consideration of Gencell preliminary motion 4, and for the reasons given, it is

ORDERED that Gencell preliminary motion 4 is **dismissed** as moot.

Upon consideration of Gencell preliminary motion 5, and for the reasons given, it is

ORDERED that Gencell preliminary motion 5 is **dismissed** as moot.

Upon consideration of Gencell/Kovesdi joint preliminary motion 1, and for the reasons given, it is

ORDERED that Gencell/Kovesdi joint preliminary motion 1 is **denied**.

Upon consideration of Kovesdi preliminary motion 1, and for the reasons given, it is

ORDERED that Kovesdi preliminary motion 1 is **dismissed** as moot.

Upon consideration of Gencell/Kovesdi joint preliminary motion 2, and for the reasons given, it is

ORDERED that Gencell/Kovesdi joint preliminary motion 2 is **granted**.

RICHARD TORCZON
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

SALLY GARDNER LANE
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

Enc.: Exhibit 1500 -- A copy of the "**RESPONSE AND AMENDMENT UNDER 37 CFR § 1.111**" filed May 8, 1996.

MICROBIOLOGY: An Introduction, by Tortora et al., pp. 321-22 (The Benjamin/Cummings Publishing Company, Inc., Menlo Park California) (1982) (copy attached).

104,829 (via overnight delivery):

Kovesdi
(real party in interest
GENVEC, INC.):

John Kilyk, Jr., Esq.
Bruce M. Gagala, Esq.
Jeffrey B. Burgan, Esq.
Heather R. Kissling, Esq.
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite4900
180 N. Stetson Ave.
Chicago, IL 60601
Tel: 312-616-5600
Fax: 312-616-5700
E-mail: JKilyk@leydig.com
BGagala@leydig.com
JBurgan@leydig.com
HKissling@leydig.com

Gencell/Perricaudet/Vigne
(real party in interest
GENCELL, S.A.):

Rochelle K. Seide, Esq.
James J. Maune, Esq.
BAKER BOTTS LLP
30 Rockefeller Plaza, 44th Floor
New York, NY 10112-4498
Tel: 212-408-2626
Fax: 646-282-9695